REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

As stated in the Office Action Summary, claims 1 and 18-27 were pending in this application when last examined. Claims 1 and 18-27 stand rejected. Claims 18-19 are amended herein to depend from claim 27. Claim 1 is canceled. Applicants reserve the right to file a continuation or divisional application directed to any subject matter deleted by way of the present Amendment.

Objection to the Specification

Applicants respectfully request that these objections continue to be held in abeyance until there is an indication of allowable subject matter.

Priority Date

Applicants note that acknowledgment has been made for the claim of domestic priority under 35 U.S.C. §§ 120 and 121. However, the Examiner maintains that the filing date of the instant claims is the filing date of the priority application, PCT/US96/18807, filed November 21, 1996, and that the earlier filed priority applications do not provide written support for the instant invention. Specifically, the Examiner asserts that the priority applications do not provide support for the manufacture of a medicament for treating rheumatoid arthritis.

Applicants submit that the presently claimed invention should be accorded the benefit of the filing date of U.S. Patent No. 5,840,299 ("the '299 patent"), November 21, 1995.

The '299 patent provides a method of treating an inflammatory disease in a patient comprising administering to the patient a therapeutically effective amount of pharmaceutical composition. The inflammatory disease may be rheumatoid arthritis, as disclosed in the specification. Specifically, the '299 patent teaches a method of treating a disease by administering a pharmaceutical composition containing the humanized monoclonal antibody 21.6. The '299 patent further discloses that the humanized MAb 21.6 is useful for treating rheumatoid arthritis ("RA"). *See* the '299 patent, column 14, line 55 to column 15, line 2. Thus, the '299 patent discloses a pharmaceutical composition comprising said humanized MAb that is useful for treating RA.

As amended, the presently claimed invention is directed to methods of treatment of rheumatoid arthritis by administering humanized MAb 21-6. Consequently, Applicants' prior application reasonably conveys to one skilled in the art that the Applicants had possession of a medicament and/or pharmaceutical composition comprising the humanized MAb useful for treating RA. Applicants again submit that there is more than adequate support for the claims of the instant application, drawn to a method of using the humanized MAb 21.6 for manufacturing a medicament for treating RA.

The claims must be given their broadest reasonable interpretation consistent with the specification. *See In re Hyatt*, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). Applicants also note that every patent is presumed to be valid. 35 U.S.C. § 282. As the '299 patent has issued, with claims directed to a method of treating an inflammatory disease in a patient, wherein the inflammatory disease may be rheumatoid arthritis, Applicants submit that there is descriptive support for the present invention in the '299 patent.

Thus, for the reasons set forth above, the instant claims should be accorded the

priority benefit of, at least, the November 21, 1995 filing date.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1 and 18-26 stand rejected under 35 U.S.C. § 112, second paragraph, as purportedly indefinite. Claims 1 and 18-26 are rejected because they purportedly recite a use without any active, positive step. In the interest of expediting prosecution, claim 1 is deleted herein, and claims 18-26 are amended to depend on claim 27. Thus, this rejection is moot.

Rejections under 35 U.S.C. § 103

Claims 1 and 18-27 remain rejected under 35 U.S.C. § 103(a) as purportedly unpatentable over Wayner et al. (U.S. Patent No. 5,730,978) in view of Bendig et al. (WO 95/19790). Applicants respectfully traverse this rejection for the reasons previously set forth, and for the reasons discussed herein below. Wayner et al. is cited for purportedly disclosing methods of suppressing immune responses to diseases including rheumatoid arthritis with a $\alpha 4\beta 1$-specific, chimeric monoclonal antibodies, though Wayner et al. do not disclose the 21.6 antibody of the claimed invention. Bendig et al. is cited for purportedly disclosing the 21.6 antibody of the claimed invention. Applicants traverse.

Before turning to the cited references, Applicants note that the claims are amended herein to depend on claim 27, and therefore recite a method of treatment of rheumatoid arthritis.

As set forth in M.P.E.P § 2142, in order to establish a *prima facie* case of obviousness, three criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings, (2) there must be a

reasonable expectation of success, and (3) the prior art references must teach or suggest all the claim limitations. As previously argued, the cited references fail to meet these requirements.

The cited references fail to provide at least the requisite suggestion/motivation to either modify and/or combine the reference teachings to arrive at the claimed invention. To this end, Applicants again submit that there are noted differences between MS and RA, and that, at the time of the claimed invention, EAE and MS were not predictive for RA.

Specifically, at the time of the claimed invention, as well as now, MS and RA were considered to be two completely different diseases with divergent etiologies and symptoms. MS is a chronic demyelinating autoimmune disease characterized by inflammatory lesions along the myelin sheath of nerve fibers in the central nervous system ("CNS"), and is localized in the CNS. An animal model of MS can be created by inducing EAE in an animal. EAE is induced by immunizing an animal with the myelin basic protein. However, the etiology of human MS had not been completely elucidated at the time of the claimed invention and still remains unknown today.

In contrast, RA is an autoimmune disease that attacks connective tissue, primarily in the joints. In this disease condition, the immune system targets the cell lining in joints, not the cells of the nervous system as in MS. As previously argued, RA is believed to be caused by a yet unknown combination of genetic, environmental, hormonal, and reproductive factors. Despite intensive research, the cause of RA remains obscure.

Thus, no meaningful scientific similarity can be drawn between MS and RA at the time the invention was filed, or today. Correspondingly, a skilled artisan at the time would not have considered that a model for one would be a suitable model for the study of or predictive efficacy for the other. The skilled artisan at the time of the claimed invention

would have reasonably believed that MS is different and distinguishable from RA. Certainly, the skilled artisan would not have concluded MS (or EAE) to be analogous to RA. As such, EAE models and methods of treatment for MS would not have been predictive for RA.

The cited references also fail to provide a reasonable expectation of success. Because MS and its animal EAE model were/are not predictive for RA, the skilled artisan would not have a reasonable expectation of success in combining and/or modifying the references to arrive at the claimed invention.

Finally, Applicants again submit that the rejection employs an "obvious to try" standard, which is improper. One cannot base a determination of obviousness on what one of ordinary skill in the art might try or find obvious to try. *In re O'Farrel*, 7 U.S.P.Q.2d 1673, 1681 (Fed. Cir. 1988). As the cited references fail to even suggest the treatment of rheumatoid arthritis, the skilled artisan would not have been led attempt to treat rheumatoid arthritis from the combination of the cited references. At best, it would merely have been "obvious to try".

Applicants respectfully request the withdrawal of this rejection.

CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

In the event any further fees are due to maintain pendency of this application, the Examiner is authorized to charge such fees to Deposit Account No. **02-4800**.

Respectfully submitted,

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